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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Maria Kebeler

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EXAMINER

HIBBERT, CATHERINE S

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/537,075	Applicant(s) KEBELER ET AL.	
	Examiner CATHERINE HIBBERT	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/14/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

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Detailed Action

Please note that the Examiner for this Application has changed. Applicants Amendment to the Specification filed 22 December 2008 is received and entered. Applicants Amendment to the Claims filed 22 December 2008 is received and entered. Applicants submittal of an Information Disclosure Statement filed 14 January 2009 has been considered. Claims 1-15 are pending and under examination.

Response to Amendment

The objection to the specification has been withdrawn based on the amendment to the specification.

35 USC 103(a) Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11 and 13-15 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Wilms et al. in view of Moralejo et al. for reasons of record and presented herein.

Applicants arguments have been fully considered but are respectfully not found persuasive. Applicants claim a method for expressing nucleic acid sequences in prokaryotic host cells (such as *E. coli*), where:

a) at least one DNA construct which is capable of episomal replication in said host cells and which comprises a nucleic acid sequence to be expressed under the transcriptional control of an L-rhamnose-inducible promoter, where said promoter is heterologous with regard to said nucleic acid sequence, is introduced into said host cells and

b) prokaryotic host cells which comprise said DNA construct in episomal form are selected and

c) the expression of said nucleic acid sequence is induced by addition of L-rhamnose to a culture of said selected host cells, wherein the prokaryotic host cell is at least deficient with regard to L-rhamnose isomerase.

Wilms et al. (cited by applicants, Biotech. Bioengineer., 2001, Vol. 73, No. 2, pp. 95-103, see whole article, particularly the Abstract, pp. 97-98, 100, of record) teaches a method for expressing nucleic acid sequences in *E. coli* wherein circular episomal plasmids (pAW178, pBW24, less than 100K in size) are used to express a heterologous polypeptide (the enzyme L-N-carbamoylase) wherein the sequence encoding the polypeptide is operably linked to the *E. coli rha*_{BAD} promoter which comprises at least one RhaS binding site which is a functional equivalent of SEQ ID NO:5 and expression of the heterologous polypeptide is induced by addition of L-rhamnose to the culture. The host cells have the RhaB gene inactivated and the cells are used to produce a

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heterologous polypeptide enzyme, L-N-carbamoylase. Wilms et al. teaches that inactivation of the RhaB gene was desirable because it reduced consumption of the expensive inducer L-rhamnose. Wilms et al. does not teach inactivation of the L-rhamnose isomerase gene in the host cell.

Moralejo et al. (cited by applicants, J. Bacteriol., 1993, Vol. 175, No. 17, pp. 5585-5594, see whole article, particularly Fig. 1, first full paragraph on p. 5591, of record) teaches the gene cluster encoding the enzymes for L-Rhamnose metabolism in *E. coli*. Moralejo et al. teaches the gene encoding the rhamnose isomerase (RhaA) (functional equivalent of SEQ ID NO:9) and that inactivation of this gene would be expected to block any catabolism of L-rhamnose.

The claimed invention is essentially described by Wilms et al. The only difference involves the inactivation of the host cellular RhaA gene. Wilms et al. inactivated the host cellular RhaB gene in order to reduce the consumption of the expensive inducer L-rhamnose whereby the normal rhamnose catabolism pathway in the cell is inhibited.

The ordinary skilled artisan, seeking to develop a method for production of heterologous polypeptides in prokaryotic cells, would have been motivated to use the method disclosed by Wilms et al. and modify said method by inactivating the RhaA gene because Moralejo et al. teaches that inactivation of the RhaA gene would be expected to block any catabolism of L-rhamnose in the cell, thereby greatly reducing the amount of the expensive inducer L-rhamnose needed to induce the expression of the recombinant polypeptide.

It would have been obvious for the ordinary skilled artisan to do this because inactivation of the RhaA gene in the host cells would greatly reduce the amount of L-rhamnose needed to induce the recombinant expression of the polypeptide of interest in the cell and thereby reduce the cost of using the system exemplified by Wilms et al.

Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention because Moralejo et al teach that rhaA mutants (isomerase deficient) were expected to block any catabolism of L-rhamnose at the time of the invention (above) and Wilms et al teach a method for expressing nucleic acid sequences encoding heterologous polypeptides in *E. coli* wherein the sequence encoding the polypeptide is operably linked to the *E. coli* rha_{BAD} promoter which comprises at least one RhaS binding site which is a functional equivalent of SEQ ID NO:5 and where expression of the heterologous polypeptide is induced by addition of L-rhamnose to the culture. The host cells have the RhaB gene inactivated and the cells are used to produce a heterologous polypeptide enzyme.

Applicants response is that Applicant argues

Moralejo does not remedy the deficiencies of Wilms. Moralejo describes identification of the open reading frames corresponding to rhaB, rhaA, and rhaD by sequencing of a fragment complementing mutations in the structural genes (Moralejo, abstract). Moralejo further discloses that only the rhaB leader region functions as a promoter and that mutations in the genes were used to show that L-rhamnose may directly induce rhaBAD transcription. Id. Thus, Moralejo does not teach or suggest a method for expressing nucleic acid sequences in prokaryotic host cells or a host cell which is deficient with regard to L-rhamnose isomerase which comprises a DNA construct comprising a nucleic acid to be expressed under the transcriptional control of an L-rhamnose-inducible promoter

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where the promoter is heterologous with the nucleic acid as required by the claims. Further, Wilms does not teach inactivation of the L-rhamnose isomerase gene in the host cell, as acknowledged by the Examiner, and Wilms also does not teach a host cell which is deficient with regard to L-rhamnose isomerase as required by the claims.

Thus, Applicants argue that “because Wilms and Moralejo, alone or in combination, do not teach or suggest all the claim limitations, a *prima facie* case of obviousness has not been established.

In addition, Applicant disagrees that it would be obvious to modify the method of Wilms by inactivating the RhaA gene rather than the RhaB gene to greatly reduce the amount of L- rhamnose needed. Applicants argue that

Wilms also describes the pathway for metabolism of L-rhamnose. Wilms discloses that L-rhamnose is taken up by *E. coli* via the permease RhaT, isomerized to L-rhamnulose by the isomerase RhaA, phosphorylated by the rhamnulose kinase RhaB to rhamnulose-1-phosphate and finally hydrolyzed by the aldolase RhaD. (Wilms, p. 95, right column, lines 25-38). The products produced are consumed by other metabolic pathways. Further, Wilms discloses that the genes RhaB, A, and D form an operon controlled by the rhaBAD promoter and that expression is strictly controlled by a regulatory cascade consisting of two regulatory proteins, RhaS and RhaR. *id.* Moreover, Wilms specifically teaches preference for the mutation in the RhaB gene because phosphorylation of L-rhamnulose by the RhaB gene is the first irreversible step in the degradation of L-rhamnose to dihydroxyacetone phosphate and L-lactaldehyde. (Wilms, p. 98, left column, lines 4-8). Wilms further teaches that this expression system takes advantage of the strictly regulated rhaBAD promoter. (Wilms, p. 95-96, right column, last sentence). Moreover, as stated in the International Preliminary Examination Report (IPER), the RhaB negative-strain is recommended especially for fermentations carried out as batch fed processes. (See English translation of IPER, p. 3, of record). Thus, Wilms disregards using any other enzyme as a potential target.

Thus, Applicants argue that Wilms and Moralejo are not combinable.

Furthermore, Applicants argue that “the isomerase RhaA catalyzes the reaction of L-rhamnose to L-rhamnulose and the rhamnulose kinase RhaB catalyzes the reaction

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of L-rhamnulose to rhamnulose-1-phosphate. The isomerase RhaA and the rhamnulose kinase RhaB relate to different parts of the pathway and they are totally different enzymes which catalyze totally different reactions". Thus, Applicants argue that "One skilled in the art would not substitute inactivation of a L-rhamnulose kinase with inactivation of a L-rhamnose isomerase" and furthermore argue that "neither Wilms nor Moralejo teach or suggest the desirability of such a substitution". Thus, Applicants argue that "Wilms and Moralejo do not render the claims obvious for these additional reasons".

Furthermore, Applicants argue that "assuming *arguendo* the references were combined, the claims are not *prima facie* obvious over Wilms in view of Moralejo, since the Examiner has failed to provide any basis for establishing that these references can be combined as proposed with a reasonable expectation of success". Applicants argue that "Since no basis has been provided that inactivation of a L-rhamnulose kinase can be substituted by the inactivation of a L-rhamnose isomerase with a reasonable expectation of success, the Examiner has failed to establish that the claims are *prima facie* obvious", stating that "Simply stating that a skilled artisan would have had a reasonable expectation of success lacks the specificity required to support a legal conclusion of obviousness and is thus insufficient to establish *prima facie* obviousness for this additional reason". Furthermore Applicants argue

there would be no expectation of success that a deficiency with regard to L-rhamnose isomerase could be used based on Wilms and Moralejo teaching a mutant with inactivated L-rhamnulose kinase, because of the differences in enzymes, in reactions catalyzed, and the strictly regulated rhaBAD promoter.

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In addition, Applicant traverse that "Assuming *arguendo* that the Examiner had established a *prima facie* case of obviousness, a *prima facie* case of obviousness is rebuttable by evidence that the claimed invention possesses unexpectedly advantageous or superior properties. *In re Papesch*, 315 F.2d 382 (CCPA 1963)", stating

The present invention relates to an improved method for expressing nucleic acids in prokaryotic cells using the rhaBAD promoter where surprisingly small quantities of L-rhamnose give high expression levels. (Specification, page 5, lines 1-4). The present method provides a particularly efficient reduction of rhamnose metabolism. In the present method, surprisingly, even rhamnose concentrations of as little as 0.04 g/L maintain, during induction in the fermenter, an extraordinarily high induction (see Figure 1 and Examples 5 and 8). For example, Example 8.2 shows that, in contrast to the effect of the rhamnose consumption observed by Wilms, the knocking-out of the isomerase leads to a virtually complete switching-off of the metabolism of the rhamnose in the fermenter.

Applicant thus notes in the footnote (1) that

in Example 8.2, the difference of the cited rhamnose concentrations at the beginning and at the end of the fermentation (0.58 g/L and 0.44 g/L, respectively) must be attributed only to the dilution of the fermenter liquor (starting volume 10 L + 200 ml preculture) by glycerol feeding (2805 g glycerol solution (80%) = 2.34 L ; =1.2 g/L) and titration with ammonia water (1.0 L) to a final volume of 13.54 L (comparison of the amount of rhamnose: $rm_{start}=0.58 \text{ g/L} \times 10.2 \text{ L}=5.9 \text{ g}$; $rm_{end}=0.44 \text{ g/L} \times 13.54 \text{ L}=5.9 \text{ g}$).

Thus, Applicants agree that

In contrast to the low amount of rhamnose needed by the present invention, Wilms describes that a substantially higher concentration of rhamnose has to be used (Wilms, p. 100, left column, and Figure 6). Figure 6 in Wilms shows that a concentration of 0.5 g/L rhamnose leads to a tailing-off of the induction after as little as 8 hours. Further, Wilms teaches that "[a]t the concentration of 0.5 g L⁻¹, the rhamnose was almost completely taken up from the cells [...]." Further Wilms teaches that only with the addition of 2 g/L rhamnose was it possible to maintain induction over a prolonged period: "A rhamnose concentration of 2 g L⁻¹ seemed to be optimal." (Wilms, p. 100, left column, and Figure 6). Consequently, a sufficient expression of a gene controlled according to Wilms is not ensured at a concentration of less than 2 g/L in the fermenter. Thus, the present method

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differs substantially from that described by Wilms. As such, even if the Examiner had established that the claims are *prima facie* obvious over the combination of Wilms and Moralejo, this *prima facie* case would be successfully rebutted by the unexpected and superior results achieved from using the claimed process with a host cell deficient with regard to L-rhamnose isomerase when compared with the system of Wilms with a totally different enzyme, L-rhamnulose kinase. (See also specification at p. 6, lines 7-43, for further advantages of the present method).

Therefore, Applicants conclude that “because Wilms and Moralejo, alone or in combination, do not teach all the claim limitations, because the reactions taught by Wilms and Moralejo are different from the claimed process, because Wilms and Moralejo are not combinable, and because assuming *arguendo* they were combinable there is no expectation of success, a *prima facie* case of obviousness has not been established”. Furthermore, Applicants argue that “assuming *arguendo* that a *prima facie* case of obviousness had been established the unexpected results successfully rebut any finding of *prima facie* obviousness. See *In re Fine*, 837 F.2d 1071, 1076 (Fed. Cir. 1988) (holding that if an independent claim is nonobvious then any claim dependent therefrom is nonobvious)”.

Applicants arguments have been fully considered but are not persuasive for reasons of record and presented herein.

Specifically, in response to applicant's argument that Wilms and Moralejo, alone or in combination, do not teach or suggest all the claim limitations and/or are not combinable, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would

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have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, The ordinary skilled artisan, seeking to develop a method for production of heterologous polypeptides in prokaryotic cells, would have been motivated to use the method disclosed by Wilms et al. and modify said method by inactivating the RhaA gene because Moralejo et al. teaches that inactivation of the RhaA gene would be expected to block any catabolism of L-rhamnose in the cell, thereby greatly reducing the amount of the expensive inducer L-rhamnose needed to induce the expression of the recombinant polypeptide.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a particular nucleic acid sequence rather than a sequence representing a biological equivalent; specific growth parameters; specific levels of L-rhamnose inactivation) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Therefore, in view of the foregoing, the method of Claims 1-11 and 13-15, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims stand properly rejected under 35 USC §103(a).

Claim 12 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Wilms et al. in view of Moralejo et al. as applied to Claim 1 above and further in view of Israelsen et al. for reasons of record and presented herein.

Applicants invention is as recited in the above 35 USC 103(a) rejection. In addition, applicants recite that the nucleic acid sequence encoding the recombinant protein is selected from the group consisting of chymosins, proteases, polymerases, saccharidases, dehydrogenases, nucleases, glucanases, glucose oxidases, α -amylases, oxidoreductases, peroxidases, laccases, xylanases, phytases, cellulases, collagenases, hemicellulases, lipases, lactases, pectinases, amyloglucosidases, glucoamylases, pullulanases, glucose isomerases, nitrilases, esterases, nitrile hydratases, amidases, oxygenases, oxynitrilases, lyases, lactonases, carboxylases, collagenases, cellulases, serum albumins, factor VII, factor VIII, factor IX, factor X, tissue plasminogen factors, protein C, von Willebrand factors, antithrombins, erythropoietins, colony-stimulating factors, cytokines, interleukins, insulins, integrins, addressins, selectins, antibodies, antibody fragments, structural proteins, collagen, fibroins, elastins, tubulins, actins, myosins, growth factors, cell-cycle proteins, vaccines, fibrinogens and thrombins.

Wilms et al. and Moralejo et al. are applied as in the above 35 USC 103(a) rejection. Wilms et al. and Moralejo et al. do not recite the recombinant protein as being one of the members of the Markush group recited in claim 12.

Israelsen et al. (US Patent 5,837,509, see whole document, particularly column 13) recites the well known and widely practiced use of recombinant bacteria to express recombinant proteins of interest such as proteases, nucleases, lipases, etc. It is noted that the Israelsen et al. reference is one among thousands of references reciting the use of recombinant bacteria to express genes of interest.

The ordinary skilled artisan, seeking to choose proteins of interest to express using the expression system disclosed by Wilms et al. and Moralejo et al., would have been motivated to choose proteins such as proteases, nucleases, lipases, etc. because Israelsen et al. teaches that recombinant bacteria can be used as hosts for expression of such proteins. It would have been obvious for the ordinary skilled artisan to do this because recombinant bacteria had been used for decades to express hundreds of different proteins of interest, as exemplified by Israelsen et al. It is further noted that any of the proteins recited in claim 12, would have been obvious to the ordinary skilled artisan as recombinant bacteria had been used to express any/all of the recited proteins. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Applicants response is to traverse the rejection stating that “the explanations provided above under obviousness rejection over Wilms and Moralejo are equally applicable to this rejection and are incorporated herein in their entirety”. In addition, Applicants argue that “as explained above, because Wilms and Moralejo, alone or in combination, do not teach all the claim limitations, because the reactions taught by Wilms and Moralejo are different from the claimed process, because Wilms and Moralejo are not combinable, and because assuming *arguendo* they were combinable there is no expectation of success, a *prima facie* case of obviousness has not been established. Furthermore, assuming *arguendo* that a *prima facie* case of obviousness had been established, the unexpected results successfully rebut any finding of *prima facie* obviousness”. Also, Applicants argue that “Claim 12, the only claim rejected under this obviousness rejection, is a dependent claim. In *In re Fine*, 837 F.2d 1071, 1076 (Fed. Cir. 1988), the court held that if an independent claim is nonobvious then any claim dependent therefrom is nonobvious. Because the independent claim is not part of this obviousness rejection, then the claims dependent therefrom are likewise nonobvious”.

Applicants response has been fully considered but is not found persuasive for reasons of record and for reasons provided above as applied to the rejection of the independent Claim 1. As the independent Claim 1 stands rejected as unpatentable over Wilms in view of Moralejo, the dependent Claim 12 also stands rejected as Wilms in view of Moralejo, as applied to Claim 1, above, and further in view of Israelsen et al.

Therefore, in view of the foregoing, the method of Claim 12, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claim stands properly rejected under 35 USC §103(a).

Conclusion

No Claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHERINE HIBBERT, Ph.D., whose telephone number is (571)270-3053. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph.D., can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/NANCY VOGEL/
Primary Examiner, Art Unit 1636
Respectfully submitted,

Catherine S. Hibbert
Examiner/AU1636